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Evaluation of the proteinuria - Creatininuria ratio for the diagnostic confirmation of preeclampsia in congolese pregnant women

Passy Kimema Nyota[1], Dophie Tshibuela Beya[1], Placide Cyanga Ngandu[1], Aliocha Nkodila Natuhoyila[2], Blaise Sumbu Matondo Manzambi[1], Mamy Ngole Zita[1], Gustave Ilunga Ntita[1], Mireille Nganga Nkanga[1], Jérémie Muwonga Masidi[1], Donatien Kayembe Nzongola-Nkasu[1], Fons Verdonck[3], Bernard Spitz[4], Jean Pierre Elongi Moyene[5]*

[1]Département de Biologie Médicale, Service de Biologie Clinique, Cliniques Universitaires de Kinshasa, Kinshasa, Republique Democratique du Congo

[2] Département de Médecine interne, Cliniques Universitaires de Kinshasa, Kinshasa, Republique Démocratique du Congo

[3] Department of Physiology, KU Leuven, Belgium

[4] Department of Gynecology-Obstetrics, KU Leuven, Belgium

[5]Département de Gynécologie-Obstétrique, Hôpital Général de Référence de Kinshasa, Kinshasa, Republique Démocratique du Congo

Abstract

Context: Preeclampsia is a multisystem endothelial disease characterized by hypertension of pregnancy and glomeruloendotheliosis resulting in significant proteinuria. These days, the weight determination of urinary proteins by 24-hour proteinuria (P24) remains the reference method for biologically confirming this condition. However, the completion of the exam appears to be very burdensome with a long waiting period for results. Hence the need to use a simple alternative method such as the proteinuria / creatininuria ratio (PCR). **Aims:** Improve the diagnosis and management of preeclampsia by using a simple, less restrictive but reliable diagnostic method. **Methodology:** The study compared the results obtained from P24 versus PCR in confirming the diagnosis of preeclampsia in 149 Congolese women in whom the disease was suspected thanks to the urine dipstick. The cut-off values used for the diagnosis of preeclampsia were, for P24, a proteinuria> 300 mg / 24 h and for PCR a value> 30 mg / mmol. **Results:** Of the 149 pregnant women in whom the diagnosis of preeclampsia was suspected using the urine dipstick, only 85.9% had a P24> 300 mg. This diagnostic confirmation rate was similar to that obtained with PCR (86.6%). A linear correlation was found between P24 and PCR in the quantification of proteinuria and in the diagnosis of preeclampsia (r^2 = 0.627, p <0.004). Comparing the pathological values diagnosed by the two methods, the agreement was 89.1% (kappa = 0.767). The PCR showed an excellent predictive performance of maternal-fetal complications at the optimal threshold of 30.8 mg / mmol corresponding to a sensitivity of 96.6% and a specificity of 95% (Youden index 0.866). This threshold was 323 mg / 24h corresponding to a sensitivity of 84% and a specificity of 61.9% (Youden index 0.459) for P24. **Conclusion:** PCR seems to be a good alternative to P24 in confirming the diagnosis of preeclampsia in the settings most affected by this pathology..

Keywords: Preeclampsia, Diagnosis, P24, PCR, Kinshasa.

INTRODUCTION

Preeclampsia is one of the major causes of maternal and perinatal morbidity and mortality in the sub-Saharan Africa countries where severe forms of the disease predominate, requiring rapid diagnosis in order to adopt consistent management, which could contribute to the improvement of the maternal and fetal prognosis often threatened in this context. It is a multisystem endothelial disease causing glomeruloendotheliosis with significant loss of protein through the urine [1]. Biological confirmation of the diagnosis of preeclampsia is based on the presence from the 20th week of gestation of proteinuria > 300 mg per 24 hours in a pregnant woman previously known to be hypertensive or with novo hypertension. In current practice, screening for this significant proteinuria is done using a urine dipstick (BU), a simple and inexpensive method but with a significant rate of false positive and false negative results up to 19% and 18% depending on the studies [2]. Currently, the gold standard for confirmation of significant proteinuria remains the proteinuria weight dosage measured over 24 hours. However, the relevance of this test during pregnancy has also been questioned by many authors, in particular due to the cumbersome nature of the procedure linked on the one hand to the need for a complete collection of urine over 24 hours and on the other hand, to the long waiting period for the result which can delay treatment. In addition, the non-compliance of certain pregnant women as well as the difficulty of emptying the bladder following ureteral compression by the pregnant uterus, especially in the third trimester, can be the cause of errors

***Corresponding author:**
Jean Pierre Elongi Moyene
Département de Gynécologie-Obstétrique, Hôpital Général de Référence de Kinshasa, Kinshasa, Republique Démocratique du Congo
Email: elongi2002[at]yahoo.fr

in the collection of urine and distort the result [3, 4, 5]. Hence the need to resort to other reliable and less restrictive alternatives to confirm the diagnosis often in an emergency context. It appears that the determination of PCR on a urine grab sample may be a better alternative to P24. The method is widely used in nephrology and appears attractive because of its speed and the ease of its implementation. It avoids errors due to variability in urine concentration and could therefore be an interesting alternative to screening for significant proteinuria (> 150 mg / day). In the study by Ginsberg *et al* [6], an excellent correlation was noted between PCR in urine sample and 24-hour proteinuria with a coefficient r = 0.972. The International Society for the Study of Hypertension in Pregnancy (ISSHP) concluded in 2000 that an PCR greater than or equal to 30 mg / mmol would be more effective than the urine dipstick and equivalent to 24-hour proteinuria [7]. The College of Obstetricians and Gynecologists of the United Kingdom (RCOG) has developed clinical practice guidelines for preeclampsia, confirming a significant correlation between an PCR greater than or equal to 30 mg / mmol and proteinuria greater than 300 mg per 24 hours [8]. Since then, several meta-analysis studies have been carried out with the objective of evaluating the performance of PCR compared to 24-hour proteinuria for the laboratory diagnosis and the rapid management of severe forms of preeclampsia, especially in the most vulnerable and affected settings.

We conducted a study to evaluate the PCR and seek its interest in the diagnosis and in the assessment of the maternal-fetal prognosis during preeclampsia in a low-income environment such as in Kinshasa, a cosmopolitan city of nearly 10 million inhabitants where the prevalence of preeclampsia is estimated at 8.3% with a predominance of severe forms [9].

MATERIAL AND METHOD

This is multicentric analytical study with recruitment taking place from January to March 2021 at the''Hopital Général de Kinshasa, Cliniques universitaires de Kinshasa and Hopital Saint Joseph de Kinshasa'' the several centers in Kinshasa at the Democratic Republic of Congo.

The study population consisted of all pregnant women who presented to ANC in the health facilities selected for this purpose during our study period and were included pregnant women suspected of preeclampsia who gave their approval. We excluded from this study pregnant women with a history of nephropathy, diabetes mellitus and those with urinary tract infections confirmed by a cytobacteriological examination of the urine. The study compared the results of P24 considered to be the gold standard in the weight measurement of proteinuria and those of PCR in the diagnosis of preeclampsia and in the prediction of associated complications. Preeclampsia was suspected in any pregnant woman previously known to be hypertensive or with the novo arterial hypertension (SBP ≥ 140mmHg and DBP ≥ 90mmHg) from the 20th year onwards associated with qualitative proteinuria at 2+ or more on the urine dipstick.

A total of 149 pregnant women were selected in whom the suspicion of preeclampsia had been advanced on the basis of pregnancy-induced hypertension associated with qualitative proteinuria by the urine dipstick (≥ 2+). The Confirmation of the diagnosis was made by quantitative research for significant proteinuria via 24-hour urine protein weight determination (P24) (criteria of the National High Blood Pressure Education Program of United States) [10] and by concomitant calculation of PCR.

The proteinuria assay was performed by the pyrogallol red colorimetric technique, a simple, economical and precise method [11]. The cut-off values were those adopted by the Working Group of the National Program of Education on Arterial Hypertension and the Working Group on Arterial Hypertension in Pregnancy, namely a proteinuria level> 300 mg / 24h for the diagnosis of preeclampsia and a rate> 3 g / 24 h for the definition of severe forms of the disease [12,13].

The PCR was calculated from the proteinuria value obtained on a punctual urine sample taken during the appointment set for pregnant women for the 24-hour urine collection and from the creatininiuria value (in mmol /l), which was carried out by the colorimetric technique according to the Jaffé method on the same sample [14]. To avoid any bias in the interpretation of the results of creatininiuria, and in accordance with the recommendations of the American conference of governmental industrial hygienists, we retained for this study only samples of pregnant women with serum creatinine values greater than 0.5 mg / dl and less than 2 mg / dl, reference values. The cut-off values for PCR were those included in the work of Bejjani *et al* [15], namely the value of 0.3 g / mmol for the diagnosis of moderate forms of preeclampsia and 2 g / mmol for the definition of the forms of severe preeclampsia.

Statistical Analyzes

The data obtained were entered on a computer using Excel 2010 software and then analyzed with SPSS version 21 software. Tables or graphs were used, as appropriate, for the presentation of the results. The continuous quantitative variables with Gaussian distribution were presented as mean ± standard deviation; those with non-normal distribution as median (extremes). Qualitative variables were described as relative frequency (%). Comparison of proportions, medians and means was performed using Chi-square test, Mann Whitney Wilcoxon U test, and Student's t test, respectively. The diagnostic performance between the different methods was achieved using Blat-Atalman curves. Se sensitivity, Sp specificity, negative VPN predictive value and positive PPV predictive value were used to assess the predictive performance of PCR and P24h with use of ROC curve to determine the threshold for complications of PCR and P24.

A value of p <0.05 was considered the threshold of statistical significance.

RESULTS

A total of 149 pregnant women were part of this study. Table I shows the socio-demographic characteristics of these pregnant women. The mean age of pregnant women was 30.6 ± 6.7 (16-45) years, the majority of pregnant women were pauciparous (mean parity 1.8 ± 0.6).

Table 1: Sociodemographic characteristics of pregnant women

Variables	Numbers (n=149)	Percentage	x ± SD (range)
Age (years)			30.6±6.7(16-45)
16-25	32	21.5	
26-35	80	53.7	
36-45	37	24.8	
Civil status			-
Married	119	79.9	
Single	30	20.1	-
Parity			1.8±0.6 (0-9)
Nulliparous	33	22.1	
Primiparous	47	31.5	
Multiparous	69	46.3	
Gestity			3.4±1.02 (1-10)
Primigest	37	24.8	
Multigest	112	75.2	
Abortion			1.1±0.8 (0-6)
No	75	50.3	
Yes	74	49.7	

As noted in Table II, a large number of these pregnant women presented signs of seriousness on admission, including signs of eclamptic prodrome (intense headache, dizziness, blurred vision, epigastralgia bar) found in 70.5% of pregnant, chest pain (7.4%), convulsions (6.0%) and dyspnea (3.4%). Overweight and obesity were reported in 35.6% and 19.5% of these pregnant women, respectively. Only 4% of pregnant women had a history of previous preeclampsia. The majority (92.6%) had a mono-fetal pregnancy.

Table 2: Clinical characteristics of patients

Clinical signs on admission, history and type of pregnancy

Variables	Numbers (n=149)	Percentage
Admission signs		
Headache	65	43.6
Fear of heights	15	10.1
Blurred vision	13	8.7
Epigastralgia	12	8.1
Chest pain	11	7.4
Convulsion	9	6.0
Dyspnea	5	3.4
Antecedents		
Overweight	53	35.6
Obesity	29	19.5
HTA	8	5.4
PE	6	4.0
Asthma	2	1.3
Diabetes	1	.7
Sickle cell anemia	1	.7
Pregnancy type		
Mono fetal	138	92.6
Twin	11	7.4

HTA: Arterial Hypertension, PE: Preeclampsia

Table III shows the clinical data on admission. The mean gestational age was 34.2 ± 4.8 WA (20.0-42.0 WA), the BMI (early pregnancy) at 26.3 ± 4.6 Kg / m^2 (19.2-46.1 Kg / m^2). The mean SBP was 163.5 ± 22.6 mm Hg (140.0-230.0 mm Hg). DBP at 106.8 ± 15.8 mm Hg (90.0-160.0 mm Hg) and MBP at 125.7 ± 17.1 mm Hg (107.0-183.0 mm Hg).

Table 3: Vital signs and anthropometric parameters

Variables	x±SD	Me (EIQ)	Min-max
Gestational age (weeks)	34.2±4.8	35.0(31.0-38.0)	20.0-42.0
BMI (Kg/m^2)	26.3±4.6	25.4(23.2-28.4)	19.2-46.1
SBP (mm Hg)	163.5±22.6	160.0(150.0-170.0)	140.0-230.0
DBP (mm Hg)	106.8±15.8	100.0(90.0-120.0)	90.0-160.0
MBP (mm Hg)	125.7±17.1	120.0(113.2-133.5)	107.0-183.0

BMI: Body Mass index, SBP: Systolic Blood Presure, DBP: Diastolic Blood Presure, MBP: Midle Blood Presure.

A high rate of cases of severe preeclampsia (45.6%) was noted although the majority of these pregnant women presented with moderate preeclampsia (54.4%) as shown in the figure below (Figure 1)

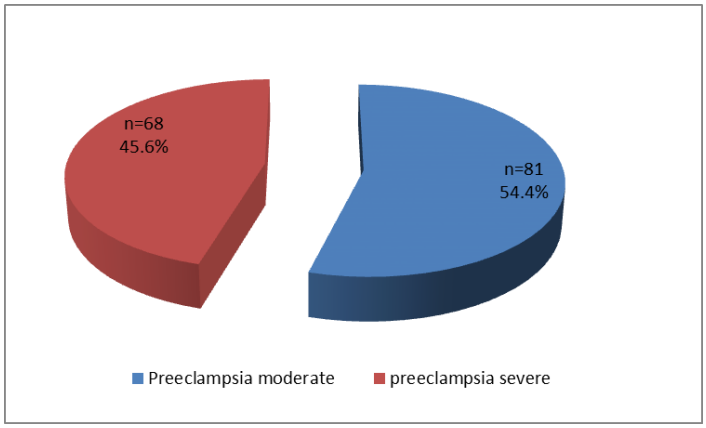

Figure 1: Type of Preeclampsia

The various complications (fetal, maternal and adnexal) observed in these pregnant women are listed in Table IV below. On the fetal side, prematurity, in utero fetal death, restriction of fetal growth and acute fetal distress among the major complications of preeclampsia while on the maternal and adnexal side, eclampsia and Placental abruption were the most common complications.

Table 4: Fetal-maternal complications

Complications	Numbers (n=149)	Percentage
Fetal complications		
Prematurity	35	23.5
fetal death	17	11.4
fetal growth retardation	16	10.7
fetal asphyxia	10	6.7
Maternal and adnexal complications		
Eclampsia	28	18.8
Placental abruption	9	6.0
Encephalopathy	6	4.0
Retinopathy	3	2.0
Pulmonary edema	3	2.0

The profile of the biological parameters for these pregnant women is thus summarized in the table below (Table V). The average rate of 24-hour proteinuria (P24) had returned to 2032.9 ± 1444.8 mg / 24h (213-6275 mg / 24h), the creatininiuria mean at 1.8 ± 1.7 mmol / l (0.4-14.8 mmol / l) and proteinuria / creatininiuria ratio (PCR) at the mean value of 176.7 ± 150.4 mg / mmol (8.3-807.4 mg / mmol).

Table 5: Biological characteristics of patients

Variables	X ± SD	Me(EIQ)	Min-Max
Point proteinuria (mg/l)	219.7±128.7	250.2(99.4-316.2)	12.3-679.0
Creatininuria (mmol/l)	1.8±1.7	1.4 (0.9-1.9)	0.4-14.8
P24 (mg24h)	2032.9±1444.8	1608.0(662.0-3179.5)	213-6275
PCR (mg/mmol)	176.7±150.4	126.3(64.9-246.4)	8.3-807.4

Figure 2 provides information that by setting the threshold for quantitative proteinuria at a value> 300 mg / 24h), we discover that on the all of these 149 pregnant women admitted for preeclampsia, only 85.9% met the definition of preeclampsia. In 14.1% of pregnant women, proteinuria remained below the value of 300 mg despite having high blood pressure.

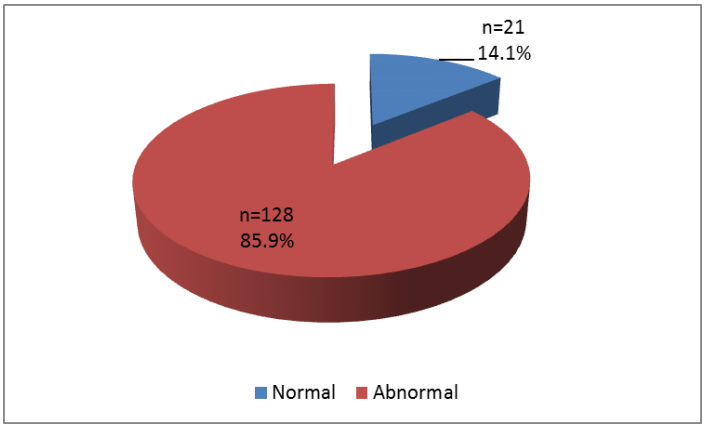

Figure 2: P24h value in the study population

Likewise, the analysis of Figure 3 below shows that of the 149 pregnant women admitted for preeclampsia from qualitative proteinuria (dipstick assay), only 86.6% had significant pathological quantitative proteinuria when resorting to the calculation of the PCR.

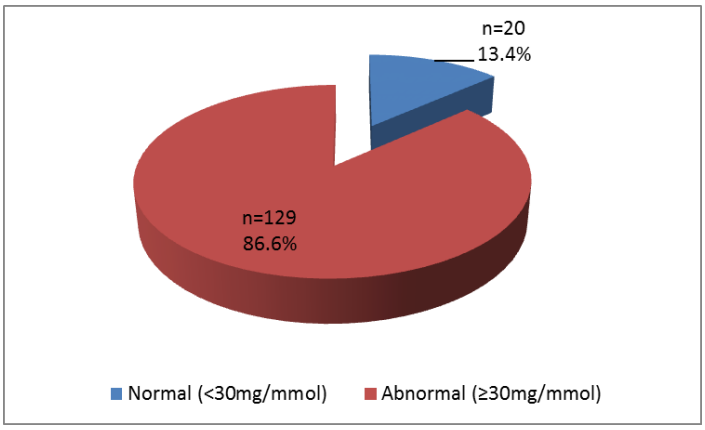

Figure 3: Value of PCR in the study population

It emerges from the analysis of the results of Table VI below that in the quantitative measurement of proteinuria for the diagnosis of preeclampsia, the calculation of the PCR was well in agreement with the P24 (kappa = 0.767),

Table 6: Diagnostic agreement between 24 hour proteinuria and PCR

	P24h		
PCR	Normal (<300mg/24)	Disturbed (≥300 mg/24)	Total
Normal (<30mg/mmol)	7	13	20
Disturbed (≥30 mg/mmol)	14	115	129
Total	21	128	149

	P24			
	Correlation (r^2)	concordance	kappa	p
PCR	0.627	89.1	0.767	0.004

The performance in confirming the diagnosis of preeclampsia was sought for each of these methods used in the assay of proteinuria, namely the qualitative method (strip assay) and the PCR by comparing them to the results obtained by the P24 which remains the gold standard in the quantification of daily proteinuria. The Bland and Altman plots (Figures 4 and 5) below established to look for bias or errors in diagnosis show that the bias between P24h and PCR was 18.6 mg / mmol with a standard deviation of 22.5 and a precision varying between 16.3 and 20.8 mg / mmol. This bias becomes significant when using the proteinuria strip (116.2 mg) with a standard deviation of 154.9 and a precision of 91-139.7 mg.

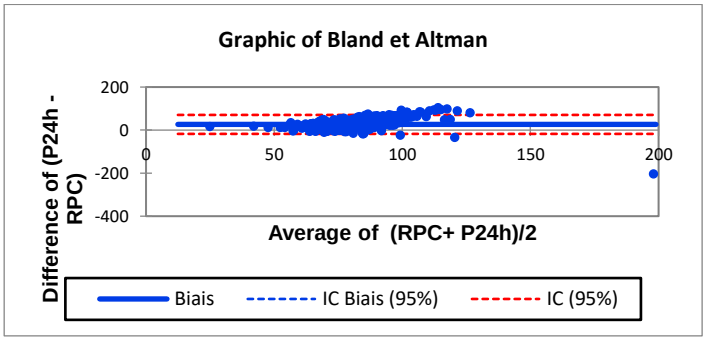

Figure 4: Method performance in the diagnosis of preeclampsia: PCR versus P24h

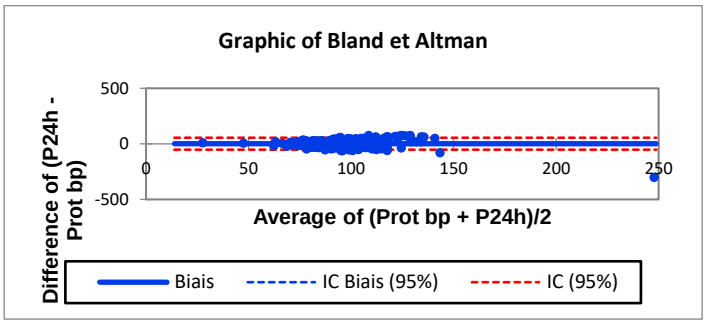

Figure 5: Performance of the Methods in the diagnosis of preeclampsia: Strip proteinuria versus P24h

The maternal, fetal and adnexal complications found with these preeclampsia pregnant women were compared to the values of the PCR in order to establish, to find the sensitivity and the specificity of the method in the prediction of these complications. Table 8 shows these different complications as a function of the RPC values. These results show that a significant number of fetal (44.2%) and maternal (38%) complications occurred in pregnant women with PCR ≥30 mg / mmol. Regarding fetal complications, the contingency table (Table 9) establishes for PCR a sensitivity (Se) of 96.6%, 95% CI (91.0-100.0), a specificity (Sp) of 90, 0%, 95% CI (80.5-99.6), a positive predictive value (PPV) of 44.2%, 95% CI (21.5-66.9) and a negative predictive value (NPV) of 20, 0% 95% CI (7.1-47.1). The precision in the diagnostic approach is excellent (Youden index at 0.866).

Table 7: Complications depending on PCR value

Variables	**Normal (<30mg/mmol) n=20**	**Disturbed (≥30 mg/mmol) n=129**	**p**
Fetal complications			**0.003**
No	18(90.0)	72(55.8)	
Yes	2(10.0)	57(44.2)	
Type of complications			
Fetal growth retardation	3(15.0)	13(10.1)	0.366
fetal death	3(15.0)	14(10.9)	0.407
fetal asphyxia	2(10.0)	8(6.2)	0.399
Prematurity	4(20.0)	31(24.0)	0.470
Maternal and adnexal complications			**0.002**
No	19(95.0)	80(62.0)	
Yes	1(5.0)	49(38.0)	
Type of complications			
Eclampsia	2(10.0)	26(20.2)	**0.022**
Retinopathy	3(15.0)	0(0.0)	

Encphalopathy	0(0.0)	6(4.7)	-
Pulmonary edema	1(5.0)	2(1.6)	0.353
Placental abruption	1(5.0)	8(6.3)	

Table 8: Prediction of PCR in fetal and maternal complications

Contingency table

Complications	PCR		Total
	Disturbed	Normal	
Yes	57	2	59
No	72	18	90
Total	129	20	149

Contingency table results

Measures	%	IC95%
Se	96.6	91.0-100.0
Sp	90.0	80.5-99.6
PPV	44.2	21.5-66.9
NPV	20.0	7.1-47.1
Youden Index	0.866	75.5-97.7

Regarding maternal and adnexal complications, the contingency table below (Table 10) establishes a sensitivity (Se) of 98.0% for PCR, 95% CI (93.7-100.0), specificity (Sp) of 95.0%, 95% CI (88.2-100.0), a positive predictive value (PPV) 38.0% 95% CI (14.1-61.9) and a negative predictive value (NPV) 19.2%, 95% CI (8.0-46.5). The precision in the diagnostic approach is excellent (Youden index at 0.930).

Table 9: Maternal and adnexal complications

Contingency table

Complications	PCR		Total
	Disturbed	Normal	
Yes	49	1	50
No	80	19	99
Total	129	20	149

Contingency table results

Mesures	%	IC95%
Se	98.0	93.7-100.0
Sp	95.0	88.2-100.0
PPV	38.0	14.1-61.9
NPV	19.2	8.0-46.5
Youden index	0.930	85.0-100.0

While searching the predictive performance of optimal threshold of P24 and RPC to discriminate maternal-fetal complications in preeclamptic patients, we note in this study that with an area under the curve of 0.690 [95% CI (0.567-0.814)], the 24-hour proteinuria presents a good predictive performance of maternal-fetal complications with an optimal threshold of 323 mg / 24h corresponding to a sensitivity 84% and a specificity of 61.9% (Youden index 0.459).

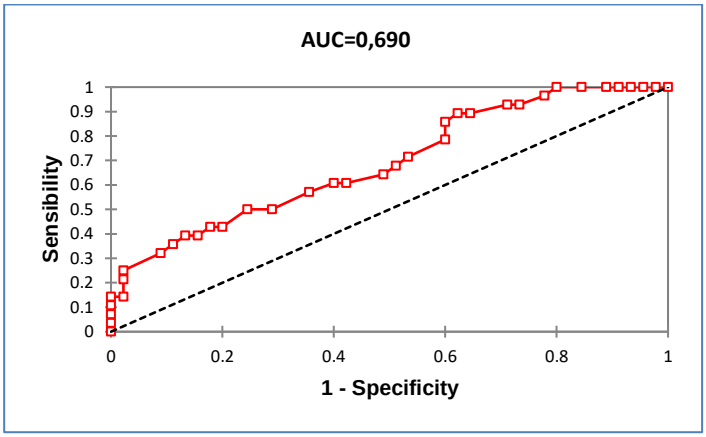

Figure 6: ROC curve Predictive performance of maternal-fetal complications and optimal threshold of P24

Referring to the PCR, we note a curve of 0.72 [95% CI (0.616-0.823)], the PCR has a good predictive performance of maternal-fetal complications at the optimal threshold of 30.8 mg / mmol corresponding to a sensitivity of 96.6% and a specificity of 95% (Youden index 0.866).

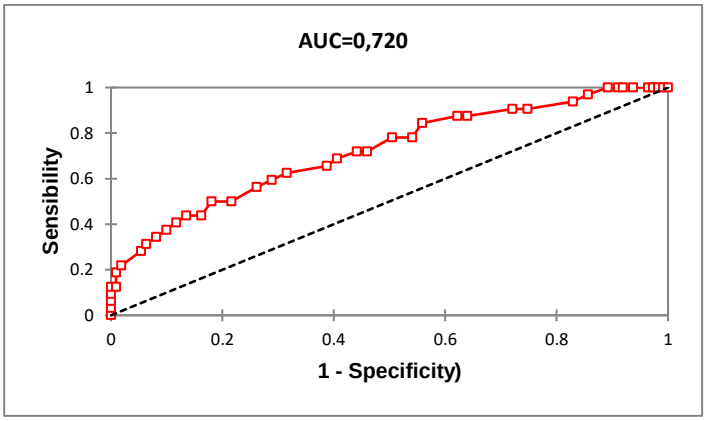

Figure 7: ROC curve Predictive performance of maternal-fetal complications and optimal threshold for PCR.

DISCUSSION

Preeclampsia is a multisystem endothelial disease causing glomeruloendotheliosis with significant loss of protein through the urine. It remains one of the major causes of maternal and perinatal morbidity and mortality in countries of sub-Saharan Africa where its prevalence can reach up to 20% of cases [16, 17]. In these countries, the majority of pregnant women do not attend qualified antenatal consultations; severe forms of the disease predominate requiring rapid diagnosis to allow consistent management, which would contribute to improving the maternal and fetal prognosis, which is often threatened in this context [18, 19]. Biological confirmation of the diagnosis of preeclampsia is based on the presence from the 20th week of gestation of proteinuria ≥ 300 mg per 24 hours, in a pregnant woman previously known to be hypertensive or with the novo arterial hypertension, this which makes it possible to exclude other forms of non-proteinuric hypertension of pregnancy of less serious prognosis [20, 21].

Thus, quantification of proteinuria remains an important step not only in establishing a diagnosis, but also in predicting maternal and fetal outcome in this condition. Today, the weight dosage of proteinuria measured over a 24 hours (P24) remains the gold standard for measuring proteinuria and diagnosing preeclampsia. However, in poor areas, such as in Sub-Saharan Africa, carrying out this examination seems expensive, very restrictive, too cumbersome and with a long waiting period for results for a pathology for which the most care must be done urgently. Hence the need to resort to simpler alternative

methods. The results of several studies [22, 23] show that the determination of PCR in a random urine sample would be an interesting alternative for quantifying proteinuria in pregnancy and confirming the biological diagnosis of preeclampsia and its complications. It is a facilitated method that can be performed quickly, which could improve the management and prognosis of the mother and the fetus in preeclampsia.

We carried out a study to highlight the interest of the determination of the PCR in the confirmation of the biological diagnosis and in the appreciation of the maternal-fetal prognosis during preeclampsia in a low-income environment such as in Kinshasa, a cosmopolitan city of nearly 10 million inhabitants where the prevalence of the disease is estimated at 8.3% with a predominance of severe forms [9]. The study compared the results obtained from two methods (P24 versus PCR) in the confirmation of the biological diagnosis of preeclampsia in 149 pregnant Congolese women in whom the diagnosis of the disease had been suspected thanks to the urine dipstick (2+ or more). The proteinuria assay was performed by the pyrogallol red colorimetric technique, a simple, economical and precise method [11, 24]. The cut-off values of P24 used in this study are those adopted by the Working Group of the National Program of Education on Arterial Hypertension, and the Working Group on Arterial Hypertension in Pregnancy, namely a proteinuria level > 300 mg / 24 h for the diagnosis of preeclampsia and a rate> 3 g / 24 h for the definition of severe forms of the disease [20, 21].

The PCR is the ratio between the value of proteinuria measured in a grab sample of urine taken during the 24-hour urine collection period over the value of creatininiuria (mmol / l) which was measured by the colorimetric technique according to the Jaffé method [14]. To avoid any bias in the interpretation of the results of creatininiuria, and in accordance with the recommendations of the American conference of governmental industrial hygienists, only samples of pregnant women with serum creatinine values greater than 0.5 mg / dl and less than 2 mg / dl were selected for this study. Regarding the cut-off values of RPC, we referred to the study by Bejjani *et al* [15] which includes 5 important meta-analyzes concerning PCR in the diagnosis of preeclampsia and its complications. It appears from these different studies that the threshold of 0.3 g / mmol (30 mg / mmol) is the best to make the diagnosis while 2 g / mmol (200 mg / mmol) would be the threshold to define the severity of the disease.

We noted during this study that of the 149 pregnant women in whom the diagnosis of preeclampsia had been suspected thanks to the urine dipstick, the confirmation of the diagnosis was only made in 85.9% of them, in which we noted a significant proteinuria> 300 mg during the 24 hour proteinuria weight assay. In 14.1% of pregnant women, the diagnosis of preeclampsia was not established by the P24 proteinuria weight assay, although qualitative proteinuria was noted in urine dipstick research. Indeed, although the screening for proteinuria by urine dipstick is a fast, easy to perform and inexpensive method, it nevertheless presents significant false-positive and false-negative rates estimated at up to 19% according to prospects comparative studies [2]. In general, the sensitivity for the urine dipstick visual test varies widely from 51% to 85%. Several factors can influence the test strip analysis including maternal hydration status, diurnal variation in protein excretion, orthostatic proteinuria, exercise, presence of infection and other contaminants in the urine such as phosphates. Thus, even a trace of proteinuria can be reported as significant if the mother is dehydrated and vice versa if the mother is too hydrated [25, 26]. Numerous studies consider that the weight determination of proteins in a urine sample collected over a 24-hour period (P24) is the gold standard in the detection of proteinuria and in the biological diagnosis of preeclampsia.

This method confirmed the diagnosis of preeclampsia in 85.9% pregnant women in the present study. Although P24 is the reference method in the quantification of proteinuria and in the diagnosis of preeclampsia, it nevertheless presents many drawbacks which could limit its practice, in particular the sluggishness in its realization which can delay the diagnosis and the treatment. The P24 also has many errors related to urine collection, storage difficulties, sample handling and poor patient compliance and may even be unnecessary when an urgent delivery is required due to the worsening of maternal and fetal condition. In the study by Coté *et al* [12], it emerge that the twenty-four hour urine collection is often inaccurate and does not give an accurate measurement of proteinuria or creatinine clearance, resting in a supine position can lead to stagnation of urine in the pelvis system- kidney so that the volume of urine collected does not reflect the actual secretion over 24 hours. Faced with these difficulties, many alternatives have been proposed for the substitution of P24. Somanathan *et al* [27], Wongkitisophon [28] noted in their studies that proteinuria of 2 hours, 4 hours could validly replace 24-hour proteinuria in the process aimed at confirming the diagnosis of preeclampsia. More recently, the use of spot tests such as proteinuria / creatininuria ratio in a random urine sample has been proposed as an alternative to P24. The method would be faster and unaffected by changes in urine concentration or the amount of urine excreted in 24 hours [29].

In the course of the present study, we have used the calculation of the PCR by fixing its significance level at 30 mg / mmol. The method confirmed the diagnosis of preeclampsia in 86.6% of these pregnant women. This diagnostic confirmation rate is very similar to that found with P24 which was 85.9%. A linear correlation was noted between 24 hour proteinuria and PCR in the determination of quantitative proteinuria and in the diagnosis of preeclampsia ($r^2 = 0.627$, $p < 0.004$). By comparing the pathological values diagnosed by the two methods, we noted an agreement of 89.1% between the two diagnostic methods (kappa = 0.767). The Bland-Altman diagram established by referring to the gold standard P24 in order to find the bias introduced when using the urine dipstick or the PCR to quantify the proteinuria made it possible to note for PCR, a bias of 18.6 mg / mmol with a standard deviation of 22.5 and a precision varying between 16.3 and 20.8 mg / mmol. While this bias is most important when using the strip method (116.2 mg) with a standard deviation of 154.9 and an accuracy of 91-139.7 mg. Our results corroborate those obtained by numerous authors around the world. Montero *et al* [30] noted in their study an excellent correlation between P24 and PCR (r 0.91 P <0.001).

The same is true with the results published by Lamontagne *et al* [31] who found in their study an excellent correlation between P24 and PCR in the biological diagnosis of preeclampsia (r = 0.92, P <0.001). The PCR showed a sensitivity of 90%, a specificity of 100%, a positive predictive value of 100% as well as a negative predictive value of 92%. The positive likelihood ratio between PCR and P24 was estimated at 8, and that of negative likelihood at 0.45. In the results published by Kayatasa *et al* [32], it was observed a significant correlation between protein excretion over 24 hours and RPC (r = 0.828, p <0.0001), PCR showed sensitivity and specificity of 60.4% and 77.9% respectively. The positive predictive value (PPV) was 77.5% and the negative predictive value (NPV) was 60.9%. Hossaina *et al* [33] noted in their study that PCR is strongly correlated with P24 in confirming the diagnosis of preeclampsia (r = 0.81, P value <0.000). Sanchez- Ramos *et al* [34] evaluated the diagnostic performance of PCR on urine sample compared to 24-hour proteinuria in a meta-analysis of 24 published studies involving 3186 patients at risk of preeclampsia. Sensitivities for PCR ranged between 67.4% and 100% and specificities between 40.9% and 100%, with averages of 91.0% and 86.3% respectively. The mean of the positive likelihoods was 6.7 and that of the negative likelihoods was 0.10. The authors concluded that PCR is a useful test for eliminating significant proteinuria in patients at risk for preeclampsia and that the threshold of 30 mg / mmol is associated with better sensitivity and specificity.

Although our results corroborate those of the authors cited above, however differ from those published by the studies of Durnwald *et al* [5] as well as those of Aggarwal *et al* [35] who noted a very weak

correlation between P24 and PCR in confirming the diagnosis of preeclampsia. The correlation coefficients found in these two studies were 0.41 and 0.596, respectively, suggesting that PCR is not a good predictor of significant proteinuria in patients with preeclampsia. However, these authors recognized the bias introduced during the performance of these studies, that related to the time of urine collection for the determination of PCR. In fact, in these two studies, urine collection for the calculation of PCR was not concomitant with P24. This urine sample was taken even before the start of urine collection for P24 and did not take into account the extent of variation in 24-hour proteinuria during preeclampsia. More recently, in a review of the literature of 5 meta-analyzes concerning PCR in the diagnostic process in case of suspected preeclampsia, Bejjani *et al* [15] find two important thresholds for PCR. The first set at 0.3 g / mmol would be the best cut off for the diagnosis of moderate forms of preeclampsia with sensitivity at 92.2% (95% CI = 89-95.3) and excellent PPV at 96.6 % (95% CI = 54.5-98.8), thus making it possible not to misdiagnose preeclampsia. The second threshold is set at 2 g / mmol for the diagnosis of severe forms of preeclampsia. It has a specificity of 96.2% (95% CI = 87-96.4) and a 94.1% PPV (95% CI = 90-97.3), which makes it possible not to ignore severe preeclampsia. Numerous studies thus show the usefulness of this method for evaluating proteinuria. Several international organizations, including the International Society for the Study of High Blood Pressure in Pregnancy, the Society of Obstetric Medicine of Australia and New Zealand, and the Society of Obstetricians and Gynecologists of Canada have adopted the measurement of this report on a sample spot urinary tract as a reasonable method of identifying significant proteinuria during pregnancy [36, 37].

We noted in the present study a high rate of maternal, fetal and adnexal complications mainly eclampsia (18.8%), prematurity (23.5%), fetal death in utero (11.4%), intrauterine growth retardation (10.7%), and placental abruption (6%). These complications have been observed in pregnant women with PCR values> 30 mg / mmol.

Regarding the prediction of these complications, the contingency table established for PCR with reference to P24 showed a sensitivity of 98.0%, 95% CI (93.7-100.0), a specificity of 95, 0%, 95% CI (88.2-100.0), and excellent precision in the diagnostic approach of maternal complications (Youden index at 0.930). As for the prediction of fetal complications, we noted a sensitivity of 96.6%, 95% CI (91.0-100.0), a specificity of 90.0%, 95% CI (80.5-99.6) and excellent precision in the diagnostic approach (Youden index at 0.866). The results of the studies by Dong *et al* [38] and many other authors [39-41] show that the severity of preeclampsia is related to the amount of proteinuria and that the risk of the occurrence of both maternal and fetal complications increases with increasing importance of it. To date, many authors have noted the usefulness of PCR not only for the diagnostic approach of preeclampsia, but also for predicting the occurrence of complications at different thresholds of proteinuria. Demirci *et al* [42], Shahbazian *et al* [43] note in their studies that the incidence of low birth weight infants is strongly associated with the importance of proteinuria. This is the case with the results published by Özkara *et al* [44] as well as by other authors [38-41] which note an association between the importance of proteinuria and the occurrence of complications during preeclampsia.

However, there is no unanimity on the protein excretion threshold value above which maternal and / or fetal complications are likely to be present. We established the ROC curve to study performance and find the optimal threshold for predicting complications for P24 and PCR. We noted for the P24 a curve of 0.690 [95% CI (0.567-0.814)] is a good predictive performance of complications with an optimal threshold of 323 mg / 24h corresponding to a sensitivity of 84% and a specificity of 61.9 % (Youden index 0.459). For PCR, we noted a curve of 0.72 [95% CI (0.616-0.823)] is an excellent predictive performance of maternal-fetal complications at the optimal threshold of 30.8 mg / mmol corresponding to a sensitivity of 96, 6% and a specificity of 95% (Youden index 0.866). Based on these results, it should therefore be noted that in our settings, complications may already appear for 24-hour proteinuria and PCR values close to the diagnosis threshold values. Hence the interest of a rapid diagnosis for a consistent support. The mean maternal age in the present study was 30.2 ± 6.7 (16-45). Pregnant women with higher PCR values were predominantly those aged 26 to 35 years (68%) (P = 0.024) and those carrying pregnancies less than 34 weeks (30.6 ± 7.3 vs 34.8 ± 4.0, P = 0.000). These data corroborate those published by Chan *et al* l [45] note in their study that in women with preeclampsia, the probability of occurrence of an unfavorable maternal outcome is significantly associated with a higher PCR at the time of diagnosis (P <0, 0001) as well as at an older maternal age (P = 0.014) whereas the increased risk of an adverse fetal outcome is associated with high PCR, a gestational age <34 weeks and systolic blood pressure ≤ 115 mmHg at the start of pregnancy.

CONCLUSION

Preeclampsia still remains one of the major causes of maternal and perinatal morbidity and mortality in the countries of sub-Saharan Africa. These days, the 24-hour proteinuria weight measurement (P24) remains the only reference method used to confirm this condition biologically. However, carrying out this method is very restrictive and too cumbersome for a pathology for which the most management must be done urgently, which requires resorting to simpler alternative methods, with a shorter delivery time of results. The results of the studies show that the PCR in a punctual urine sample could represent an interesting alternative in the diagnosis of preeclampsia and its complications, because of the ease and speed of its execution. We conducted a study in a few hospitals in the city of Kinshasa province, Democratic Republic of Congo in order to highlight the interest of PCR in the diagnosis of preeclampsia. It emerges from the results of this study that the calculation of the PCR is well in agreement with the P24 (kappa = 0.767). In relation to the prediction of these maternal complications, the PCR showed a sensitivity (Se) of 98.0%, a specificity (Sp) of 95.0%, and an excellent precision in the diagnostic approach (Youden index at 0.930). We also noted for PCR a sensitivity (Se) of 96.6%, a specificity (Sp) of 90.0%, and excellent precision in the diagnostic approach prediction of fetal complications (Youden index at 0.866). The optimal threshold value of PCR for the onset of fetal-maternal complications is 30.8 mg / mmol corresponding to 323 mg / 24 h for P24, values close to the threshold values used for the diagnosis.

In view of these results, PCR appears to be a good alternative to P24 for the diagnosis of preeclampsia and for the prediction of future complications. It is a simple test, less expensive, with a shorter time to obtain results, allowing rapid management of patients.

Its introduction in the assessment of preeclampsia, replacing P24, will reduce the costs of the management of preeclampsia.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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